REMARKS

Reconsideration is requested.

The undersigned's review of the PTO IFW reveals that a Bibliographic Data Sheet indexed on May 2, 2007, and dated April 13, 2007 in the lower right corner of the Sheet, includes an acknowledgement that U.S. Serial No. 07/920,286 is a U.S. National Phase of PCT/EP91/02409, in hand-written text initialed and dated "12/31/1991" by an unidentified individual. The undersigned has requested, on more than one occasion, a Corrected Filing Receipt which includes the acknowledgement that U.S. Serial No. 07/920,286 is a U.S. National Phase of PCT/EP91/02409. See February 20, 2007 for the most recent Request in this regard. The Office is again requested to issue a Corrected Filing Receipt.

Moreover, the Bibliographic Data Sheet indexed on May 2, 2007, and dated April 13, 2007 in the lower right corner of the Sheet does not acknowledge receipt of a copy of the foreign priority claim or that the requirements of 35 USC § 119 (a-d) have been met. Correction and acknowledgement of the same in the Examiner's next Action are requested. The undersigned notes in this regard that the Examiner has acknowledged in the Office Action of May 2, 2007 receipt of the applicants priority document in the parent application. Correction of the Patent Office records with regard to the Bibliographic Data Sheet however is also requested.

The specification has been revised in the cross-reference, as requested by the Examiner on page 3 of the Office Action dated May 2, 2007.

The Rule 75 objection to claims 71-73, 77-84 and 86-89 is obviated by the above amendments. The claims have been revised according to acceptable wording suggested in MPEP § 608.01(n). Withdrawal of the objection is requested.

The Examiner is requested to hold in abeyance the obviousness-type double patenting rejection of claims 55, 59, 60, 62, 68-70 and 85 over claims 1-7, 12, 19-22, 27, 32, 33 and 38 of U.S. Patent No. 6,007,982, claims 1-6, 13-15, 22, 23, 26, 39 and 40 of U.S. Patent No. 5,910,404, claims 1-6, 13-24 and 26 of U.S. Patent No. 6,872,520, and claims 1-5, 7, 12 and 21-24 of U.S. Patent No. 5,922,532, until such time as allowable subject matter is indicated. The Examiner is requested to hold in abeyance the obviousness-type double patenting rejection of claims 55, 59, 60, 62, 68-70 and 85 over claims 1-3, 5-7, 9-11, 13-15, 17-24, 27 and 28 of U.S. Patent No. 6,287,761 and claims 1, 3, 4, 6, 7 and 9-12 of U.S. Patent No. 6,576,417, until such time as allowable subject matter is indicated. In the meantime, clarification is requested regarding the Examiner's assertion that the presently rejected claims are allegedly "anticipated by the patented invention" (see page 4 of the Office Action dated May 2, 2007) as the rejection is understood to be based on the judicially created doctrine of obviousness-type double patenting as opposed to Section 101, same type double patenting. Clarification is requested in the event the rejections are maintained.

The Section 102 and Section 103 rejection of claims 55, 59, 60, 62, 68-70 and 85 over Houghton (U.S. Patent No. 5,350,671), is traversed. Reconsideration and withdrawal of the rejections are requested in view of the following distinguishing comments.

Initially, the applicants note that the cited patent was considered by the Examiners in the parent and related U.S. Patent Nos. 5,910,404; 5,922,532; 6,287,761; 6,576,417; and 6,872,520, and the claims of U.S. Patent Nos. 5,910,404; 5,922,532; 6,287,761; 6,576,417; and 6,872,520 were found to be patentable over the cited patent. Moreover, the Examiner has asserted that the presently pending claims are allegedly obvious in view of various claims of U.S. Patent Nos. 5,910,404; 5,922,532; 6,287,761; 6,576,417; and 6,872,520. It is inconsistent for the Examiner to assert that the claims of the present application are allegedly anticipated or obvious over the cited patent while also asserting that claims which are patentable over the cited art (i.e., the claims of U.S. Patent Nos. 5,910,404; 5,922,532; 6,287,761; 6,576,417; and 6,872,520) would have made the presently claimed invention obvious.

The Examiner is requested to either withdraw the Section 102 and Section 103 rejection of claims 55, 59, 60, 62, 68-70 and 85 over Houghton (U.S. Patent No. 5,350,671) or withdraw the obviousness-type double patenting rejections of claims 55, 59, 60, 62, 68-70 and 85 over claims 1-7, 12, 19-22, 27, 32, 33 and 38 of U.S. Patent No. 6,007,982, claims 1-6, 13-15, 22, 23, 26, 39 and 40 of U.S. Patent No. 5,910,404, claims 1-6, 13-24 and 26 of U.S. Patent No. 6,872,520, and claims 1-5, 7, 12 and 21-24 of U.S. Patent No. 5,922,532; and claims 55, 59, 60, 62, 68-70 and 85 over claims 1-3, 5-7, 9-11, 13-15, 17-24, 27 and 28 of U.S. Patent No. 6,287,761 and claims 1, 3, 4, 6, 7 and 9-12 of U.S. Patent No. 6,576,417.

For completeness, the applicants again note that Houghton et al. does not contain an enabling disclosure of immunodiagnostic peptides of the Core, NS4 or NS5 region of HCV. Houghton et al. may disclose polynucleotide and polyprotein sequences

from HCV as well as recombinantly produced polypeptides. At Col 28, line 54 to Col 29, line 68, for example, Houghton et al. list an overlapping range of peptides covering the whole HCV polyprotein. At Col 28, lines 30-54, it is mentioned that the ordinarily skilled person is to screen the whole HCV polyprotein for possible truncated HCV amino acid sequences comprising epitopes. One of the techniques mentioned which can allegedly be used to help identify epitopes is computer analysis. It is, however, stressed by Houghton et al. at line 49 that:

> "It is appreciated by those skilled in the art that such computer analysis does **not** always identify an epitope that actually exists, and can also incorrectly identify a region of the protein as containing an epitope" (emphasis added).

In addition, Col 28, line 54 states that:

> "Examples of HCV amino acid sequences that **may be** useful as described herein are set forth below" (emphasis added).

It is clearly stated at lines 55-58 that:

> "these peptides do **not** necessarily precisely map one epitope, but **may** also contain HCV sequence that is **not** immunogenic" (emphasis added).

The non-immunogenic properties of the sequence of the cited art are yet to be defined. Also, the presence of an epitope in any of the sequences given in the list of the cited patent is yet to be defined. In fact, Houghton et al. is not believed to demonstrate that any of the given peptides (taken alone or used in combination) achieves the goal of being a diagnostically useful peptide. The Houghton et al. disclosure is a non-enabling disclosure as to Core, NS4 and NS5 polypeptides which are diagnostically useful or

contain epitopes. The cited patent fails to place the presently claimed invention in the public domain.

The present inventors were first to discover, after several selection procedures using overlapping synthetic 20 mer peptides spanning the whole HCV polyprotein, different diagnostically useful peptides from the HCV Core, NS4 and NS5 region, which give a positive result in HCV antibody recognition assays using antisera incubated with these peptides bound on a solid substrate. These peptides clearly possess diagnostically useful properties (see experimental section of the present application).

Houghton et al. do not demonstrate which regions of the HCV polyprotein are diagnostically preferred. Houghton et al. do not teach or suggest which peptides or combination of peptides are to be used for efficient detection of antibodies. Consequently, the use of an assay for detection of HCV incorporating a combination of any of the peptide fragments would not have been obvious over Houghton et al.

As further evidence of the patentability of the claimed invention, the Examiner is requested to see the evidence of record in the parent applications, such as the attached copies of remarks and evidence presented in the related application no. 08/466,975 (on February 4, 1998) and application no. 08/391,671 (on December 12, 1997).

Withdrawal of the Section 102 and Section 103 rejections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required in this regard.

Respectfully submitted,

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For the Examiner's convenience, the applicants note the following overview of comparisons discussed below.

SEQ ID NO:	AA # (Peptide No: according to present specification)	Compared to Houghton's AA # (alternative designation in attached tables)	Compared to Wang's AA # (alternative designation in attached tables)
9	1688-1707 (VIII) (NS4-1)	1690-1720 (NS4HOU1), 1694-1735 (NS4HOU2)	1699-1718 (NS4-W3)
10	1694-1713 (IX) (NS4-2)	1690-1720 (NS4HOU1), 1694-1735 (NS4HOU2)	1699-1718 (NS4-W3)
11	1706-1725 (X) (NS4-4)	1690-1720, (NS4HOU1) 1694-1735 (NS4HOU2)	1699-1718, (NS4-W3) 1716-1735 (NS4-W2)
12	1712-1731 (XI) (NS4-5)	1690-1720, (NS4HOU1) 1694-1735 (NS4HOU2)	1716-1735 (NS4-W2)
13	1718-1737 (XII) (NS4-6)	1694-1735, (NS4HOU2) 1720-1745 (NS4HOU3)	1716-1735, (NS4-W2) 1727-1748 (NS4-W1)
14	1724-1743 (XIII) (NS4-7)	1720-1745 (NS4HOU3)	1716-1735, (NS4-W2) 1727-1748 (NS4-W1)
15	1730-1749 (XIV)		1727-1748 (NS4-W1)

The HCV peptide sequences were synthesized as N-terminally biotinylated peptides. The procedure used is described in WO 93/18054, copy attached.

The peptides were compared by ELISA and LIA.

For ELISA, the peptides were coated directly to the plates at a concentration of 1μg/ml in PBS and all further steps were performed as stated in the INNOTEST HCV AbIII (Innogenetics, Belgium) package insert using the same reagents.

For LIA, peptides were coated directly on the membranes at a concentration of 50 μg/ml in PBS and all further steps were performed as stated in the INNO-LIA HCV Ab III

(Innogenetics, Belgium), package insert using the same reagents

To test sera for the presence of antibodies to the antigens present on the strip, the test strip was placed in a plastic trough and covered with 1 ml of PBS containing casein and Triton X705. To this was added 10 µl of the serum sample to be tested. Incubation was carried out overnight at room temperature with gentle agitation. Subsequently, the liquid was removed and the strips washed several times with the same buffer (pH 7.0) to remove any unbound antibodies. Bound antibodies were detected by incubation with a goat anti-human IgG:alkaline phosphate conjugate. Following this incubation period, the strips were washed extensively to remove any unbound conjugate. The presence of bound conjugate was detected by incubation with the substrate 5-bromo-4-chloro-3-indolyl phosphate (BCIP) in the presence of Nitro Blue tetrazolium (NBT), which is converted to a dark precipitate by the action of the enzyme.

Signals obtained with the LIA system were scored in a manner well known in the art for the commercially available INNO-LIA HCV Ab III test. Briefly, intensities are compared with a cutoff (=0.5), a 1+ control line, and a 3+ control line. Reactivites were detected in all sera as shown in Table 3.

Twenty randomly selected HCV-positive sera and 4 sera obtained from HCV-negative blood donors were taken for analysis. Assay conditions were as described in the Methods section. The Optical Density values were analyzed as follows. For each peptide, a cutoff was established based on the mean of OD values obtained with the 4 negative samples, elevated with 5 standard deviations. Such a calculation of cutoff values is common practice. The cutoff is subsequently

used to calculate signal to cutoff values (S/co). Tables 1 and 2 show the OD values and Table 2 gives the S/co values. A S/co of higher or equal to 1.0 is interpreted as positive, a S/co of <1.0 is considered negative; as is the case for most commercially available assays used for detection of infectious diseases. In most blood banks and clincial laboratories, 'greyzone' values are considered, these usually lie between S/co values of 0.8 and 1.0. Such greyzone values may indicate the presence of specific antibodies below the detection limit of the assay and are used for clinical management of the donor or patient, for example, to request a follow up sample for further confirmation. In addition, a S/co value between 1.0 and 2.0 is usually considered as weakly positive. Such weakly positive signal may be lost when the peptide is combined with other HCV peptides in a test. Based on these criteria which have been equally applied for all peptides, peptides of the invention have been compared with what the applicants submit is the closest cited art peptides.

Furthermore, it should be made clear that the immune response to HCV is multispecific. In order to detect most of the HCV-infected cases, the use of multiple epitopes is required. Therefore, an additional reactivity of one peptide with 5% of HCV positive cases is considered as a major advantage in the screening and confirmation of HCV antibodies. An overall additional detection of 1% of HCV positive cases, or even 0.1%, or only one or a few cases out of millions of blood donations, is already considered as a very competitive advantage of the assay. In this light, the detection of only 1 additional case out of 20 HCV positive sera is considered as a major advantageous property of the particular peptide.

Peptide VIII (NS4-1; 1688-1707)

Out of 20 HCV positive samples, 12 (60%) react with peptide VIII. One sample (5%) showed greyzone reactivity.

Comparison with peptides 1690-1720 and 1694-1735 based on the positions proposed by Houghton et al.

Both peptides 1690-1720 and 1694-1735 react in a very similar way with the HCV positive samples tested and in comparison with peptide VIII. However, serum samples 17758 and 17761 are both positive when tested with peptide VIII, but negative with peptide 1690-1720 and peptide 1694-1735. The latter peptide represents clone 5-1-1 which has been originally discovered by Chiron Corporation as the first recombinant clone from a phage library. The current experiment shows that certain epitopes can be presented only in the peptides of the present invention as compared to peptides of the cited art.

Comparison with peptide 1699-1718 of Wang et al.

Peptide VIII (1688-1707) shows a surprisingly high reactivity with 11/23 (48%) of HCV positive sera as compared to peptide 1699-1718 (NS4-W3) which reacts with only 3/23 sera (13%).

Peptide IX (NS4-2; 1694-1713)

Out of 20 HCV positive samples, 12 (60%) react with peptide IX. Three samples (15%) showed greyzone reactivity.

Comparison with peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2) based on the positions proposed by Houghton et al.

Both peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2) react in a very similar way with the HCV positive samples tested and in comparison with peptide IX. However, serum samples 17758 and 17761 both show positive reactivities when tested with peptide IX, but they are negative with peptide 1690-1720 and peptide 1694-1735. The latter peptide represents clone 5-1-1 which has been originally discovered by Chiron Corporation as the first recombinant clone from a phage library. The current experiment shows that certain epitopes can be presented only in the peptides of the present invention as compared to peptides of the cited art.

Comparison with peptide 1699-1718 (NS4-W3) of Wang et al.

Peptide IX (1694-1713) shows a surprisingly high reactivity with 11/23 (48%) of HCV positive

sera as compared to peptide 1699-1718 (NS4-W3)which reacts with only 3/23 sera (13%).

Peptide X (NS4-4; 1706-1725)

Out of 20 HCV positive samples, 9 (45%) react with peptide X. Four samples (20%) showed greyzone reactivity.

Comparison with peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2) based on the positions proposed by Houghton et al.

Both peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2) react in a very similar way with the HCV positive samples tested and in comparison with peptide X. However, sample 17799 is positive when tested on peptide X, but negative with both peptides 1690-1720 and 1694-1735. In addition, sample 17803 shows borderline reactivity when tested on peptide X and is not detected with peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2). Serum samples 17758 and 17761 both show greyzone reactivities when tested with peptide VIII, but are negative with peptide 1690-1720 and peptide 1694-1735. The latter peptide represents clone 5-1-1 which has been originally discovered by Chiron Corporation as the first recombinant clone from a phage library. The current experiment shows that certain epitopes can be presented only in the peptides of the present invention as compared to peptides of the cited art.

Comparison with peptide 1699-1718 (NS4-W3) and of Wang et al.

Peptide X (NS4-4; 1706-1725) showed high reactivity with sample 12451, while peptide 1699-1718 only reacted very weakly (1.34) with this sample. In addition, samples 10929 and 17764 showed greyzone reactivities with peptide X while negative on peptide 1699-1718.

Comparison with peptide 1716-1735 (NS4-W2) and of Wang et al.

Peptide X (NS4-4; 1706-1725) showed high reactivity with sample 17802, while peptide 1699-1718 showed no reactivity with this sample. In addition, samples 10929 and 17764 showed greyzone reactivities with peptide X while negative on peptide 1716-1735.

Peptide XI (NS4-5; 1712-1734)

Out of 20 HCV positive samples, 9 (45%) react with peptide XI. Seven samples (35%) showed greyzone reactivity.

Comparison with peptides 1690-1720 (NS4HOU1) and 1694-1735 (NS4HOU2) based on the positions proposed by Houghton et al.

Both peptides 1690-1720 and 1694-1735 react in a very similar way with the HCV positive samples tested and in comparison with peptide XI. However, samples 17758, 17805, and 17799 are positive when tested on peptide XI, but negative with both peptides 1690-1720 and 1694-1735. In addition, samples 17763 and 17798 both show greyzone reactivities when tested with peptide XI, but are negative with peptide 1690-1720 and peptide 1694-1735. The latter peptide represents clone 5-1-1 which has been originally discovered by Chiron Corporation as the first recombinant clone from a phage library. The current experiment shows that certain epitopes can be presented only in the peptides of the present invention as compared to peptides of the prior art.

Comparison with peptide 1716-1735 (NS4-W2) of Wang et al.

Samples 10914 and 17842 (2/23 or 9%) can be detected using peptide XI (1712-1731), while they remain negative when tested on peptide 1716-1735.

Peptide XII (NS4-6; 1718-1737)

Comparison with peptides 1694-1735 (NS4HOU2) and 1720-1745 (NS4HOU3) based on the positions proposed by Houghton et al.

Peptide XII did not show any advantages in an Elisa format over the closest prior art peptides. However, when used in a line immunoassay format (Table 3), serum 17805 was detected positive while it was indeterminate using peptide 1720-1745 and negative with peptide 1694-1735. This peptide may therefore be particularly useful for confirmatory testing.

Comparison with peptide 1716-1735 (NS4-W2) of Wang et al.

No additional reactivities of peptide XII could be observed as compared to peptide 1716-1735 in a first series of 23 patients samples (Table 5). In a second series of comparisons in using 45 HCV-positive samples, samples 17794, 17801, and 17820 (3/68 or 4.4%) were positive when tested on peptide XII while no reactivity could be detected on peptide 1716-1735 (Table 4). Furthermore, samples 17761, 17764, 17765, 17767, 17770, 17773, 17779, 17783, 17784, 17786, 17788, 17789, 17796, 17797, 17799, 17804, 17811, 17817, and 17830 (19/68 or 27.9%) showed greyzone reactivities with peptide XIII while negative on peptide 1716-1735. Overall, 22 out of 68 samples tested showed reactivities which could not be detected by the cited art peptide 1716-1735 of Wang et al.

Comparison with peptide 1727-1748 (NS4-W1) of Wang et al.

No additional reactivities of peptide XII could be observed as compared to peptide 1727-1748 in

a first series of 23 patients samples (Table 5). In a second series of comparisons using 45 HCV-positive samples, samples 17820 and 8243 (2/68 or 2.9%) were positive when tested on peptide XII while no reactivity could be detected on peptide 1727-1748 (Table 4). Furthermore, samples 17761 and 17779 (2/68 or 2.9%) showed greyzone reactivities with peptide XII while negative on peptide 1727-1748. Overall, 4 out of 68 (6%) samples showed reactivities with peptide XII which could not be detected by prior art peptide 1727-1748 of Wang et al.

Peptide XIII (NS4-7; 1724-1743)

Comparison with peptide 1720-1745 (NS4HOU3) based on the positions proposed by Houghton et al.

Peptide XIII did not show any advantages in an Elisa format over peptide 1720-1745 based on the sequence proposed to be immunoreactive by Houghton et al. (Table 2). However, when used in a line immunoassay format (Table 3), serum 17779 was dedected positive with peptide XIII while it was indeterminate using peptide 1720-1745. In addition, an indeterminate result was obtained for sample 17817 on peptide XIII while no reactivity could be detected using peptide 1720-1745. This peptide may therefore be particularly useful for confirmatory testing.

Comparison with peptide 1716-1735 (NS4-W2) by Wang et al.

Serum sample 10914 (1/23 or 4.3%) could be detected using peptide XIII while no reactivity was seen with peptide 1716-1735 of Wang et al (Table 5). In a second series of comparisons using 45 HCV-positive samples, samples 17789, 17794, and 17817 (3/45 or 6.7%) were positive when tested on peptide XIII while no reactivity could be detected on peptide 1716-1735 (Table 4). Furthermore, samples 17761, 17764, 17765, 17767, 17773, 17777, 17778, 17784, 17785, 17786, 17788, 17796, 17797, 17804, 17811, 17814, 17816, 17818, 17828, 17831, 8242, 8247, 8250, and 8330 (24/45 or 53.3%) showed greyzone reactivities with peptide XIII while negative on peptide 1716-1735. Overall, 28 out of 68 (41%) HCV samples showed reactivity with peptide XIII which could not be detected by means of prior art peptide 1716-1735.

Comparison with peptide 1727-1748 (NS4-W1) by Wang et al.

No additional reactivities of peptide XIII could be observed as compared to these peptides in a first series of 23 patients samples (Table 5). In a second series of comparisons using 45 HCV-positive samples, samples 17789, 17817, and 8243 (3/68 or 4.4%) were positive when tested on peptide XIII while no reactivity could be detected on peptide 1727-1748 (Table 4). Furthermore, samples 17761, 17785, 17818, 17821, 17831, 8242, and 8247 (7/68 or 10.3%) showed greyzone reactivities with peptide XIII while the samples were negative on peptide 1727-1748. Overall, 10 out of 68 (14.7%) HCV samples showed reactivities which could be detected with peptide XIII but which could not be picked up by means of peptide 1727-1748 of Wang et al.

Peptide XIV (1730-1749)

Comparison with peptide 1727-1748 (NS4-W1) by Wang et al.

In a small series of 23 HCV positive samples, no additional reactivities were detected for peptide XIV in Elisa as compared to peptide 1727-1748. In a line immunoassay format, however, sample 17775 showed indeterminate reactivity while no reaction was seen with peptide 1727-1748 of Wang et al. (Data not shown.)

In conclusion, from the above and attached data, which have been generated from only a limited set of HCV-positive sera, it is submitted that each of the peptides VIII, IX, X, XI, XII, XIII, and XIV possess unexpected reactivities as compared to the peptides which were synthesized based on the sequence positions suggested by Houghton et al. Peptides VIII, IX, X, XI, XII, XIII, and XIV also displayed unexpected reactivities as compared to the peptides of Wang et al. These results demonstrate the claimed invention is not obvious in view of the cited art and withdrawal of the Section 103 rejections is requested.

The claims, as amended, are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is invited to contact the undersigned if anything further is required.

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Table 1 Elisa comparison of Innogenetics NS4 peptides with positions proposed by Houghton et ...

Sample	VIII 1688-1707	IX 1694-1713	X 1706-1725	XI 1712-1731	XII 1718-1737	XIII 1724-1743	NS4HOU1 1690-1720	NS4HOU2 1694-1735	NS4HOU3 1720-1745
17758	134	89	54	62	37	37	44	48	47
17760	834	1014	649	194	36	39	1594	703	92
17761	157	104	53	38	44	48	40	43	41
17763	42	47	45	49	45	48	35	46	47
17765	1519	1767	1047	55	48	53	1237	1046	153
17767	51	41	42	42	46	40	218	40	39
17770	154	597	45	53	35	41	625	841	43
17773	1593	1826	688	42	39	52	1339	1160	139
17775	45	38	45	39	35	40	40	39	37
17779	1544	1671	860	48	35	37	1426	1229	209
17783	44	48	50	37	38	55	46	49	41
17805	38	39	51	100	37	41	47	55	39
17789	358	257	365	223	36	44	218	698	42
17798	38	43	52	49	40	49	37	41	39
17799	40	44	223	67	42	40	38	51	41
17803	39	53	65	50	39	43	49	49	40
17807	1705	905	1127	50	47	52	701	513	266
17810	1894	1918	362	47	47	49	1742	1547	45
17817	78	226	57	58	46	49	772	270	39
17818	2422	2446	1238	51	49	51	2301	2154	100
B51	51	51	53	50	51	50	48	53	51
B52	49	52	56	51	47	52	48	51	46
B53	53	50	51	51	48	47	55	54	51
B54	48	52	50	51	41	52	49	53	52
co	62.1	56.05	65.75	53.25	67.7	72.05	66.88	59.05	63.5

Table 2 ELISA comparison of Innogenetics NS4 peptides with positions proposed by Houghton et al.

Sample	VIII 1688-1707	IX 1694-1713	X 1706-1725	XI 1712-1731	XII 1718-1737	XIII 1724-1743	NS4HOU1 1690-1720	NS4HOU2 1694-1735	NS4HOU3 1720-1745	NS4-1 1688-1707	NS4-2 1694-1713	NS4-4 1706-1725	NS4-5 1712-1731	NS4-6 1718-1737	NS4-7 1724-1743	NS4HOU1 1690-1720	NS4HOU2 1694-1735	NS4HOU3 1720-1745
17758	134	89	54	62	37	37	44	48	47	2.16	1.59	0.82	1.16	0.55	0.51	0.66	0.81	0.74
17760	834	1014	649	194	36	39	1594	703	92	13.43	18.09	9.87	3.64	0.53	0.54	23.83	11.91	1.45
17761	157	104	53	38	44	48	40	43	41	2.53	1.86	0.81	0.71	0.65	0.67	0.60	0.73	0.65
17763	42	47	45	49	45	48	35	46	47	0.68	0.84	0.68	0.92	0.66	0.67	0.52	0.78	0.74
17765	1519	1767	1047	55	48	53	1237	1046	153	24.46	31.53	15.92	1.03	0.71	0.74	18.50	17.71	2.41
17767	51	41	42	42	46	40	218	40	39	0.82	0.73	0.64	0.79	0.68	0.56	3.26	0.68	0.61
17770	154	597	45	53	35	41	625	841	43	2.48	10.65	0.68	1.00	0.52	0.57	9.35	14.24	0.68
17773	1593	1826	688	42	39	52	1339	1160	139	25.65	32.58	10.46	0.79	0.58	0.72	20.02	19.64	2.19
17775	45	38	45	39	35	40	40	39	37	0.72	0.68	0.68	0.73	0.52	0.56	0.60	0.66	0.58
17779	1544	1671	860	48	35	37	1426	1229	209	24.86	29.81	13.08	0.90	0.52	0.51	21.32	20.81	3.29
17783	44	48	50	37	38	55	46	49	41	0.71	0.86	0.76	0.69	0.56	0.76	0.69	0.83	0.65
17805	38	39	51	100	37	41	47	55	39	0.61	0.70	0.78	1.88	0.55	0.57	0.70	0.93	0.61
17789	358	257	365	223	36	44	218	698	42	5.76	4.59	5.55	4.19	0.53	0.61	3.26	11.82	0.66
17798	38	43	52	49	40	49	37	41	39	0.61	0.77	0.79	0.92	0.59	0.68	0.55	0.69	0.61
17799	40	44	223	67	42	40	38	51	41	0.64	0.79	3.39	1.26	0.62	0.56	0.57	0.86	0.65
17803	39	53	65	50	39	43	49	49	40	0.63	0.95	0.99	0.94	0.58	0.60	0.73	0.83	0.63
17807	1705	905	1127	50	47	52	701	513	266	27.46	16.15	17.14	0.94	0.69	0.72	10.48	8.69	4.19
17810	1894	1918	362	47	47	49	1742	1547	45	30.50	34.22	5.51	0.88	0.69	0.68	26.05	26.20	0.71
17817	78	226	57	58	46	49	772	270	39	1.26	4.03	0.87	1.09	0.68	0.68	11.54	4.57	0.61
17818	2422	2446	1238	51	49	51	2301	2154	100	39.00	43.64	18.83	0.96	0.72	0.71	34.40	36.48	1.57
B51	51	51	53	50	51	50	48	53	51	0.82	0.91	0.81	0.94	0.75	0.69	0.72	0.90	0.80
B52	49	52	56	51	47	52	48	51	46	0.79	0.93	0.85	0.96	0.69	0.72	0.72	0.86	0.72
B53	53	50	51	51	48	47	55	54	51	0.85	0.89	0.78	0.96	0.71	0.65	0.82	0.91	0.80
B54	48	52	50	51	41	52	49	53	52	0.77	0.93	0.76	0.96	0.61	0.72	0.73	0.90	0.82
co	62.1	56.05	65.75	53.25	67.7	72.05	66.88	59.05	63.5									

Table 3 **LIA comparison of Innogenetics NS4 peptides with positions proposed by Houghton et al.**

	Peptide Sample	VIII	IX	X	XI	XII	XIII	NS4HOU1	NS4HOU2	NS4HOU3
LIA	17758	0.5	0	0	1	0	0.5	0.5	1	0.5
	17760	2	1	0	2	0	2	2	2	2
	17761	1	0	0	0	0	0	0.5	1	0
	17763	0	0	0	0.5	0	0	0	0	0
	17765	2	2	0	2	0	2	2	2	2
	17767	0	0	0	1	0	0	0	0.5	0.5
	17770	0	0	0	0.5	2	2	0	2	2
	17773	2	1	0	0	0	0	2	2	0
	17775	0	0	0	0.5	0	0	0.5	0.5	0
	17779	2	1	0	0	0	1	2	2	0.5
	17783	0	0	0	1	0.5	2	0	0.5	2
	17805	0	0	0	0	1	0	0	0	0.5
	17789	0	0	0	2	0	2	0	2	2
	17798	0	0	0	0	0	0	0	0	0.5
	17799	0	0	0	2	0	0.5	0	0.5	0.5
	17803	0	0	0	1	0	0.5	0.5	0.5	0.5
	17803	2	1	0	0	0	1	2	2	2
	17810	2	0	0	0	0	0	1	1	0
	17817	0.5	0	0	1	0	0.5	0.5	1	0
	17818	2	0.5	0	2	0	0.5	2	2	0.5
	B51	0	0	0	0	0	0	0	0	0
	B52	0	0	0	0	0	0	0	0	0
	B53	0	0	0	0	0	0	0	0	0
	B54	0	0	0	0	0	0	0	0	0

Table 4: ELISA comparisons of peptides XII and XIII with peptides spanning positions 1727-1748 and 1716-1735 of Wang et al.

	OD				S/co			
	XII 1718-1737	XIII 1724-1743	NS4 W1 1727-1748	NS4 W2 1716-1735	XII 1718-1737	XIII 1724-1743	NS4 W1 1727-1748	NS4 W2 1716-1735
IGP	186	185	1306	1307	186	185	1306	1307
17758	41	38	39	31	0.76	0.79	0.74	0.48
17759	39	28	31	29	0.72	0.58	0.58	0.45
17761	44	40	32	42	0.81	0.83	0.60	0.66
17764	45	43	51	42	0.83	0.90	0.96	0.66
17765	49	40	49	46	0.91	0.83	0.92	0.72
17767	46	45	57	42	0.85	0.94	1.08	0.66
17770	46	35	46	48	0.85	0.73	0.87	0.75
17773	52	41	46	41	0.96	0.85	0.87	0.64
17777	37	39	54	30	0.69	0.81	1.02	0.47
17778	33	41	51	35	0.61	0.85	0.96	0.55
17779	44	31	41	37	0.81	0.65	0.77	0.58
17783	43	38	45	38	0.80	0.79	0.85	0.59
17784	44	42	46	42	0.81	0.88	0.87	0.66
17785	41	41	41	35	0.76	0.85	0.77	0.55
17786	48	41	47	40	0.89	0.85	0.89	0.63
17788	51	45	49	42	0.94	0.94	0.92	0.66
17789	45	49	51	55	0.83	1.02	0.96	0.86
17790	37	32	59	40	0.69	0.67	1.11	0.63
17791	59	50	61	69	1.09	1.04	1.15	1.08
17794	60	64	132	56	1.11	1.33	2.49	0.88
17796	48	41	61	35	0.89	0.85	1.15	0.55
17797	49	39	48	40	0.91	0.81	0.91	0.63
17799	48	36	46	38	0.89	0.75	0.87	0.59
17801	54	38	54	42	1.00	0.79	1.02	0.66
17804	44	40	55	49	0.81	0.83	1.04	0.77
17805	37	27	46	57	0.69	0.56	0.87	0.89
17808	36	31	40	45	0.67	0.65	0.75	0.70
17810	38	33	44	39	0.70	0.69	0.83	0.61
17811	43	42	45	38	0.80	0.88	0.85	0.59
17814	41	39	49	41	0.76	0.81	0.92	0.64
17816	38	41	63	45	0.70	0.85	1.19	0.70
17817	45	145	51	43	0.83	3.02	0.96	0.67
17818	34	46	34	45	0.63	0.96	0.64	0.70
17820	95	37	34	63	1.76	0.77	0.64	0.98
17821	33	39	36	51	0.61	0.81	0.68	0.80
17825	38	36	46	38	0.70	0.75	0.87	0.59
17826	40	38	44	41	0.74	0.79	0.83	0.64
17828	39	40	44	39	0.72	0.83	0.83	0.61
17830	47	35	46	40	0.87	0.73	0.87	0.63
17831	42	47	37	50	0.78	0.98	0.70	0.78
8242	37	45	33	44	0.69	0.94	0.62	0.69
8243	59	57	32	107	1.09	1.19	0.60	1.67
8247	34	42	41	45	0.63	0.88	0.77	0.70
8250	37	40	45	37	0.69	0.83	0.85	0.58
8330	40	47	53	38	0.74	0.98	1.00	0.59
D1	43	39	47	37	0.80	0.81	0.89	0.58
D2	38	41	44	44	0.70	0.85	0.83	0.69
D3	38	42	45	45	0.70	0.88	0.85	0.70
co	54		48	53				64

Table 5: ELISA comparison of Innogenetics NS4 peptides with Wang et al. NS4 peptides

	INNOGENETICS							WANG		
	VIII	IX	X	XI	XII	XIII	XIV	NS4-W1	NS4-W2	NS4-W3
Ig# / Ag	1688-1707	1694-1713	1706-1725	1712-1731	1718-1737	1724-1743	1730-1749	1727-1748	1716-1735	1699-1718
17802 (1/2)	0.631	0.320	0.453	0.653	0.047	0.046	0.049	0.055	0.261	0.053
17803(1/2)	0.045	0.055	0.065	0.042	0.037	0.041	0.039	0.040	0.049	0.040
17807(1/2)	0.669	0.247	0.052	0.049	0.042	0.049	0.050	0.052	0.040	0.053
17812(1/2)	0.048	0.051	0.052	0.050	0.041	0.049	0.050	0.048	0.044	0.045
17819(1/2)	0.141	0.236	0.054	0.055	0.047	0.053	0.047	0.057	0.049	0.047
17823(1/2)	0.047	0.050	0.055	0.048	0.042	0.050	0.044	0.046	0.045	0.047
17827(1/2)	0.648	1.193	0.053	0.047	0.048	0.054	0.047	0.052	0.049	0.046
17847(1/2)	0.442	0.988	0.054	0.050	0.045	0.054	0.048	0.049	0.048	0.047
8309(1/2)	0.049	0.051	0.058	0.054	0.052	0.055	0.052	0.055	0.056	0.056
8316(1/2)	0.049	0.051	0.053	0.053	0.052	0.052	0.054	0.050	0.051	0.054
8332(1/2)	0.045	0.063	0.055	0.050	0.050	0.058	0.048	0.052	0.054	0.051
8356(1/2)	0.057	0.061	0.054	0.051	0.053	0.122	0.045	0.052	0.050	0.050
8358(1/2)	0.056	0.135	0.054	0.051	0.051	0.050	0.049	0.054	0.054	0.051
8380(1/2)	0.047	0.050	0.058	0.052	0.051	0.051	0.054	0.053	0.055	0.060
17775(1/2)	0.047	0.060	0.061	0.047	0.050	0.127	0.059	0.074	0.064	0.061
10911(1/2)	0.049	0.051	0.053	0.050	0.049	0.050	0.049	0.053	0.051	0.051
10914(1/2)	0.636	0.052	0.065	0.370	0.048	0.052	0.048	0.052	0.052	0.529
12451(1/2)	1.333	0.331	0.727	0.372	0.049	0.052	0.050	0.054	0.102	0.128
10929(1/2)	2.075	2.299	0.092	0.057	0.046	0.051	0.048	0.056	0.054	0.052
17764(1/2)	0.363	0.276	0.081	0.050	0.037	0.039	0.034	0.041	0.049	0.053
17771(1/2)	1.457	1.418	0.041	0.039	0.037	0.040	0.036	0.046	0.048	0.073
17818(1/2)	0.988	1.575	0.040	0.044	0.042	0.045	0.045	0.051	0.053	0.044
17842(1/2)	0.040	0.054	0.055	0.093	0.041	0.047	0.042	0.041	0.045	0.052
B-1	0.048	0.051	0.059	0.052	0.048	0.071	0.047	0.055	0.063	0.053
B-2	0.049	0.053	0.060	0.055	0.048	0.113	0.059	0.069	0.060	0.055
B-3	0.056	0.054	0.063	0.053	0.057	0.231	0.051	0.094	0.055	0.052
B-4	0.057	0.059	0.072	0.061	0.074	0.330	0.042	0.060	0.057	0.058
	0.076	0.071	0.093	0.075	0.118	0.773	0.086	0.156	0.076	0.068

17802 (1/2)	8.30	4.51	4.87	8.71	0.40	0.06	0.57	0.35	3.43	0.78
17803(1/2)	0.59	0.77	0.70	0.56	0.31	0.05	0.45	0.26	0.64	0.59
17807(1/2)	8.80	3.48	0.56	0.65	0.36	0.06	0.58	0.33	0.53	0.78
17812(1/2)	0.63	0.72	0.56	0.67	0.35	0.06	0.58	0.31	0.58	0.66
17819(1/2)	1.86	3.32	0.58	0.73	0.40	0.07	0.55	0.37	0.64	0.69
17823(1/2)	0.62	0.70	0.59	0.64	0.36	0.06	0.51	0.29	0.59	0.69
17827(1/2)	8.53	16.80	0.57	0.63	0.41	0.07	0.55	0.33	0.64	0.68
17847(1/2)	5.82	13.92	0.58	0.67	0.38	0.07	0.56	0.31	0.63	0.69
8309(1/2)	0.64	0.72	0.62	0.72	0.44	0.07	0.60	0.35	0.74	0.82
8316(1/2)	0.64	0.72	0.57	0.71	0.44	0.07	0.63	0.32	0.67	0.79
8332(1/2)	0.59	0.89	0.59	0.67	0.42	0.08	0.56	0.33	0.71	0.75
8356(1/2)	0.75	0.86	0.58	0.68	0.45	0.16	0.52	0.33	0.66	0.74
8358(1/2)	0.74	1.90	0.58	0.68	0.43	0.06	0.57	0.35	0.71	0.75
8380(1/2)	0.62	0.70	0.62	0.69	0.43	0.07	0.63	0.34	0.72	0.88
17775(1/2)	0.62	0.85	0.66	0.63	0.42	0.16	0.69	0.47	0.84	0.90
10911(1/2)	0.64	0.72	0.57	0.67	0.42	0.06	0.57	0.34	0.67	0.75
10914(1/2)	8.37	0.73	0.70	4.93	0.41	0.07	0.56	0.33	0.68	7.78
12451(1/2)	17.54	4.66	7.82	4.96	0.42	0.07	0.58	0.35	1.34	1.88
10929(1/2)	27.30	32.38	0.99	0.76	0.39	0.07	0.56	0.36	0.71	0.76
17764(1/2)	4.78	3.89	0.87	0.67	0.31	0.05	0.40	0.26	0.64	0.78
17771(1/2)	19.17	19.97	0.44	0.52	0.31	0.05	0.42	0.29	0.63	1.07
17818(1/2)	13.00	22.18	0.43	0.59	0.36	0.06	0.52	0.33	0.70	0.65
17842(1/2)	0.53	0.76	0.59	1.24	0.35	0.06	0.49	0.26	0.59	0.76

Even if a *prima facie* case of obviousness were established, the Applicants respectfully submit the following and attached demonstrate the claims are not obvious over the cited art. During the interview, the Examiner was unable to identify the peptides of the cited art which should be compared with the present invention. The Applicants have made the following comparison of what they believe to be appropriate, based on the length of comparable sequences disclosed in Houghton et al.

Specifically, Houghton's AA2265-AA2280 (column 29, line 50, EREISVPAEILRKSRR), AA2280-AA2290 (column 29, line 50, RFAQALPVWAR), AA2310-AA2330 (column 29, line 52, VVHGCPLPPPKSPPVPPPRKK), AA2255-AA2270 (column 29, line 49, SFNPLVAEENEREISV), and AA2290-AA2310 (column 29, line 51, RPDYNPPLVETWKKPDYEPPV) were compared with SEQ ID NO:s 16-20 (AA2263-AA2282, AA2275-AA2284, AA2287-AA2306, AA2299-AA2318, and AA2311-AA2330, respectively) of the presently claimed invention.

The HCV peptide sequences were synthesized as N-terminally biotinylated peptides. The procedure used is described in WO 93/18054, copy attached.

The peptides were compared by ELISA and LIA.

For ELISA, the peptides were coated directly to the plates at a concentration of 1μg/ml in PBS and all further steps were performed as stated in the INNOTEST HCV AbIII (Innogenetics, Belgium) package insert using the same reagents.

The attached Table 3 shows signal-to-cutoff values of 19 randomly selected samples from patients with chronic hepatitis C (20 samples taken in all). The cutoff was calculated as the mean of OD values for the 20 samples (see Table 1) obtained with blood donor sera (B51 to B54) augmented with 5 standard deviations, as is common practice to those skilled in the art. Eighteen of these 20 sera contained NS5 antibodies.

Table 2 shows results of ELISA tests. Table 3 shows results of LIA tests.

With reference to Table 2; comparing the reactivities of different sera with peptides NS5-25 (2263-2282) of the invention and peptides spanning positions 2255-2270 and 2265-2280 of Houghton et al., it can be concluded that the reactivity of the peptide of the invention is surprisingly higher for sera 17767 and 17775 than with either one of the two Houghton peptides. The peptide of the invention also reacts better with sera 17770 and 17779 than the reactivity of the 2255-2270 Houghton peptide. Upon comparing the reactivities of different sera with peptide NS5-27 (2275-2297) of the invention and peptide spanning positions 2280-2290 of Houghton et al., it can be concluded that the reactivity of the peptide of the invention is surprisingly higher for sera 17770, 17798 and 17807 than the reactivity of the Houghton peptide. Upon comparing the reactivities of different sera with peptide NS5-29 (2287-2306) of the invention and peptides spanning 2280-2290 and 2290-2310 of Houghton et al., it can be concluded that the reactivity of the peptide of the invention is surprisingly higher for sera 17761, 17765, 17767, 17770, 17773, 17775, 17798 and 17807 than the reactivity of the Houghton peptides. Upon comparing the reactivities of different sera with the NS5-31 (2299-2318) of the invention and peptides spanning positions 2290-2310 and 2310-2330 of Houghton et al., it can be concluded that the reactivity of the peptide of the invention is surprisingly higher for sera 17761, 17765, 17767, 17775, 17779, 17798, 17799, 17807 and 17818 than the reactivity of the Houghton peptides. Upon comparing the reactivities of different sera with the NS5-33 (2311-2330) of the invention and peptides spanning positions 2310-2330 of Houghton et al., it can be concluded that the reactivity of the peptide of the invention is surprisingly higher for almost all sera than the reactivity of the Houghton peptides.

Sera 17758, 17763, 17783 and 17803 (20% of sera) can be detected using the peptides of the invention, while no reactivity is observed with peptides based on the sequences proposed by Houghton.

Sera 17760, 17770, 17773, 17789, 17798, 17807, and 17810 (35% of sera) react strongly using the peptides of the invention, while only weak reactivity is observed with peptides based on the sequences proposed by Houghton

Sera 17761, 17765, 17767, 17775, 17779, and 17799 (30% of sera) react more strongly using the peptides of the invention, as compared with the reactivity is observed with peptides based on the sequences proposed by Houghton.

Serum 17818 showed a slightly higher, but comparable reactivity with peptide 2310-2330 of Houghton, as compared to the peptide 2311-2330 of the present invention.

Overall, 17/18 (94%) NS5-reactive sera showed no reactivity or weaker signal-to-cutoff values on peptides based on the sequences proposed by Houghton as compared to the peptides of the presently claimed invention.

For LIA, peptides were coated directly on the membranes at a concentration of 50 μg/ml in PBS and all further steps were performed as stated in the INNO-LIA HCV Ab III (Innogenetics, Belgium), package insert using the same reagents

To test sera for the presence of antibodies to the antigens present on the strip, the test strip was placed in a plastic trough and covered with 1 ml of PBS containing casein and Triton X705. To this was added 10 ul of the serum sample to be tested. Incubation was carried out overnight at room temperature with gentle agitation. Subsequently, the liquid was removed and the strips washed several times with the same buffer (pH 7.0) to remove any unbound antibodies. Bound antibodies were detected by incubation with a goat anti-human IgG:alkaline phosphate conjugate. Following this incubation period, the strips were washed extensively to remove any

unbound conjugate. The presence of bound conjugate was detected by incubation with the substrate 5-bromo-4-chloro-3-indolyl phosphate (BCIP) in the presence of Nitro Blue tetrazolium (NBT), which is converted to a dark precipitate by the action of the enzyme.

Signals obtained with the LIA system were scored in a manner well known in the art for the commercially avialable INNO-LIA HCV Ab III test. Briefly, intensities are compared with a cutoff (=0.5), a 1+ control line, and a 3+ control line. Reactivites were detected in 19/20 sera as shown in Table 3.

Higher LIA signals were obtained with the peptides of the present invention with 18 out of 19 (95%) reactive sera.

Sera 17760, 17763, 17783, 17805, 17810, and 17817 (30% of sera) did not react with any of the peptides based on the sequences proposed by Houghton, while they scored positive with the peptides of the presently claimed invention.

Comparable reactivities with the peptides of the present invention and with the peptides of Houghton were detected for serum 17818. Only serum 17775 showed a 3+ reactivity on the peptide based on the sequence 2310-2330 while a 2+ reactivity was obtained on the peptide 2311-2330 of the present invention.

These results demonstrate an unexpected improvement over the cited art which demonstrate the unobviousness of the presently claimed invention.

The claims, as amended, are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is invited to contact the undersigned if anything further is required.

Respectfully submitted,

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Table 1

TABLE 1

	NS5-25 2263-2282	NS5-27 2275-2294	NS5-29 2287-2306	NS5-31 2299-2318	NS5-33 2311-2330	NS5HOU1 2255-2270	NS5HOU2 2265-2280	NS5HOU3 2280-2290	NS5HOU4 2280-2310	NS5HOU5 2310-2330
17758	37	48	44	130	107	42	37	48	48	39
17760	40	39	57	627	374	120	84	68	191	45
17781	42	41	1408	1999	857	511	469	377	1487	45
17783	43	48	50	220	111	45	39	37	359	38
17785	233	50	643	2351	1120	397	473	335	939	47
17787	628	41	601	1915	162	73	670	48	48	38
17770	223	395	284	711	421	83	283	47	497	39
17773	48	48	299	624	1544	103	42	41	77	1240
17778	795	84	1262	2083	1774	888	680	301	1222	2038
17779	142	48	48	1512	584	55	180	37	972	38
17783	49	50	63	41	68	40	37	38	38	38
17805	47	50	50	44	51	43	49	38	41	48
17789	48	51	53	42	2129	121	40	38	48	1981
17798	38	1373	1401	1588	323	83	42	41	1532	38
17799	41	41	145	1198	458	197	185	58	291	37
17803	41	61	48	419	52	48	40	42	41	38
17807	52	393	1820	1347	1139	132	50	58	1434	1099
17810	51	50	54	47	205	48	38	48	48	81
17817	53	51	58	48	60	52	51	48	127	48
17818	50	50	50	1607	557	62	51	47	660	1470
BS1	51	51	51	57	49	55	50	47	58	44
BS2	51	52	53	49	50	54	51	49	63	37
BS3	48	52	48	48	50	55	58	48	547	47
BS4	51	54	52	45	60	57	50	49	1041	48
co	62.25	98.54	66.05	70.45	52.25	61.54	68.11	53.04	4303.9	66.05

Table 1

TABLE 2

	NS5-25 2263-2282	NS5-27 2275-2294	NS5-29 2287-2306	NS5-31 2299-2318	NS5-33 2311-2330	NS5HOU1 2255-2270	NS5HOU2 2265-2280	NS5HOU3 2280-2290	NS5HOU4 2290-2310	NS5HOU5 2310-2330
17758	0.59	0.79	0.67	1.70	2.05	0.68	0.66	0.87	0.01	0.55
17760	0.64	0.67	0.66	6.20	7.16	1.95	1.27	1.24	0.04	0.68
17761	0.67	0.70	21.29	26.76	16.40	8.30	7.09	7.11	0.35	0.68
17763	0.69	0.82	0.76	2.88	2.12	0.73	0.59	0.70	0.06	0.55
17765	3.74	0.85	9.74	30.75	21.44	6.45	7.16	6.32	0.15	0.71
17767	13.30	0.70	12.13	25.05	2.91	1.19	6.62	0.80	0.01	0.55
17770	3.58	6.75	4.00	9.30	8.06	1.35	3.98	0.89	0.12	0.59
17773	0.77	0.82	4.63	6.16	29.65	1.67	0.64	0.77	0.02	18.77
17775	12.77	1.09	19.11	26.98	33.95	11.18	10.44	5.67	0.28	30.86
17779	2.28	0.82	0.70	19.78	10.79	0.89	2.72	0.70	0.23	0.55
17783	0.79	0.85	0.80	0.84	1.07	0.65	0.68	0.74	0.01	0.56
17806	0.76	0.85	0.76	0.58	0.98	0.70	0.74	0.68	0.01	0.70
17789	0.77	0.87	0.80	0.66	40.76	1.97	0.61	0.72	0.01	29.99
17798	0.61	23.45	21.21	20.75	6.18	1.35	0.64	0.77	0.36	0.58
17799	0.66	0.70	2.20	16.67	8.73	3.20	2.80	1.09	0.07	0.58
17803	0.66	0.87	0.73	6.48	1.00	0.78	0.61	0.79	0.01	0.58
17807	0.64	6.71	24.53	17.62	21.72	2.14	0.76	1.06	0.33	16.64
17810	0.82	0.85	0.82	0.61	3.92	0.78	0.57	0.87	0.01	1.23
17817	0.85	0.87	0.85	0.63	0.96	0.84	0.77	0.87	0.03	0.70
17818	0.80	0.85	0.76	21.02	10.66	0.84	0.77	0.89	0.20	22.26
B51	0.82	0.87	0.77	0.75	0.94	0.89	0.76	0.89	0.01	0.67
B52	0.82	0.89	0.80	0.64	0.96	0.88	0.77	0.92	0.01	0.56
B53	0.74	0.89	0.70	0.60	0.96	0.89	0.65	0.90	0.13	0.71
B54	0.82	0.92	0.79	0.59	0.96	0.93	0.76	0.92	0.38	0.70

ELISA

Table 3

TABLE 3

	NS5-25 2263-2282	NS5-27 2275-2294	NS5-29 2287-2306	NS5-31 2299-2318	NS5-33 2311-2330	NS5HOU1 2255-2270	NS5HOU2 2265-2280	NS5HOU3 2280-2290	NS5HOU4 2290-2310	NS5HOU5 2310-2330
17760	0.5	0	0.5	2	0	0	0	0	0	0
17761	2	2	2	3	0	0	1	0	1	0
17763	2	0	0	0.5	0	0	0	0	0	0
17765	2	2	1	3	0	0	1	0	1	0
17767	2	1	1	2	0	0	1	0	0	0
17770	2	2	1	2	0	0	1	0	1	0
17773	0.5	2	0.5	2	2	0	0	0	0	2
17775	2	2	1	2	2	0.5	1	0	0.5	3
17779	2	0.5	0	2	0	0	1	0	0.5	0
17783	1	1	0	0	0	0	0	0	0	0
17805	0	1	0	0	0	0	0	0	0	0
17789	0	1	0	0	2	0	0	0	0	2
17798	0	2	2	2	0	0	0	0	1	0
17799	2	1	0.5	2	0	0.5	1	0	1	0
17803	1	1	0	2	0	0	0.5	0	0	0
17803	2	2	1	2	1	0	1	0	0	1
17810	1	1	0	0	0	0	0	0	0	0
17817	0	0	0	0.5	0	0	0	0	0	0
17818	0	0.5	0	2	0	0	0	0	0.5	2
B51	0	0	0	0	0	0	0	0	0	0
B52	0	0	0	0	0	0	0	0	0	0
B53	0	0	0	0	0	0	0	0	0	0
B54	0	0	0	0	0	0	0	0	0	0

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